Therapeutic Studies in Hyperthyroidism

Use of Radioactive Iodine

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• Of 112 patients with hyperthyroidism who were treated with radioactive iodine, 110 were relieved of the disease. Nine had transient hypothyroidism. Twelve had permanent hypothyroidism. No other adverse effects that could be attributed to radioactive iodine were noted.

On May 4, 1942, two papers were read before the American Society for Clinical Investigation reporting experiences with radioactive iodine in treating patients with hyperthyroidism.[3, 4] Since that day, a flood of papers has reported the results of many groups of investigators with this new therapeutic agent.

The Thyroid Clinic of the University of Southern California School of Medicine at the Los Angeles County General Hospital began using the eight-day half-life isotope, I^{131}, in April 1948. From that time until September 1953, the drug had been given to 394 patients—to 26 of them for the treatment of thyroid cancer.

This, the first report of the group, deals with an analysis of 112 cases of hyperthyroidism observed for from six months to five years.

MATERIAL AND METHODS

The patients were selected from the group of heterogeneous nationality treated in the Los Angeles County Hospital. Sixteen were males; 96 were females. The age range was from 15 to 85 years.

Diagnosis was established by clinical manifestations supported by physical examination, basal metabolism, determinations of protein-bound iodine in the blood, cholesterol content, radioactive iodine uptake and excretion studies, and, when indicated, measurements of the eyes with the Hertel exophthalmometer. The weight and size of the gland was estimated by palpation at the beginning and during the course of treatment.

Thirty of the patients had known they had disease for more than five years. Sixty-nine had diffuse goiter, 33 had nodular goiter, one had substernal goiter, and nine had no clinical enlargement of the gland.

Sixteen had undergone thyroidectomy before treatment with radioactive iodine; 61 had had previous medical treatment with antithyroid drugs; and six had had both.

Selected for treatment were patients who (1) were past the age of 40, or (2) had had previous operation with subsequent recurrence of the disease, or (3) were considered poor surgical risks, because of serious heart disease or other disturbances, or (4) for various reasons refused operation.

The average single dose of radioactive iodine was 7 millicuries. Patients were observed for at least eight weeks after therapy before further therapy was considered. If at the end of this time the clinical status had not improved and the protein-bound iodine level in the blood had not dropped, the person was considered for re-treatment. Second and third doses of radioactive iodine varied in amount from half to equal the initial dose, depending on the clinical problem and the results of repeated tracer studies.

RESULTS

One hundred ten patients (98.2 per cent) were relieved of hyperthyroidism. One of the two not relieved did not persevere in treatment and the other died of another disease before hyperthyroidism abated.

Ninety-eight of the group (87.5 per cent) returned to a euthyroid status; nine of these (8 per cent) were transiently hypothyroid. In 12 members of the group (10.7 per cent) there developed what appears at this time to be permanent hypothyroidism. In one patient symptoms characteristic of malignant exophthalmos developed after therapy with radioactive iodine, but it is not felt that this condition is related to the type of therapy used to control hyperthyroidism. No exact figures are available with respect to the occurrence of tenderness in the neck after therapy with I^{131}. Tenderness was noted, but never as more than a transient mild problem.

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The average total dose was 8.8 millicuries of I^{131} in patients with diffuse enlargement of the thyroid gland; for patients with nodular goiter the average was 11.03 millicuries. The variation of doses between one patient and another, however was so great (see Charts 1 and 2) that data on averages have little value. Ninety patients were treated with only one dose; 12 required two doses; and 10 required three or more doses. Of the 33 patients with multinodular goiter, 11 (or 33 per cent) required second or third treatments. Of the 69 patients with diffuse enlargement of the thyroid gland, 11 (or 16 per cent) required re-treatment. Of 61 patients who received previous treatment with antithyroid drugs, 17 (or 28 per cent) required multiple treatments with radioactive iodine. Of 36 patients who had had no previous therapy, medical or surgical, five (or 14 per cent) required multiple treatments with I^{131}. Four of 16 patients (25 per cent) who had had thyroidectomy in the past for hyperthyroidism, required multiple treatments with I^{131}. The average time of remission including those re-treated was 10 to 12 weeks.

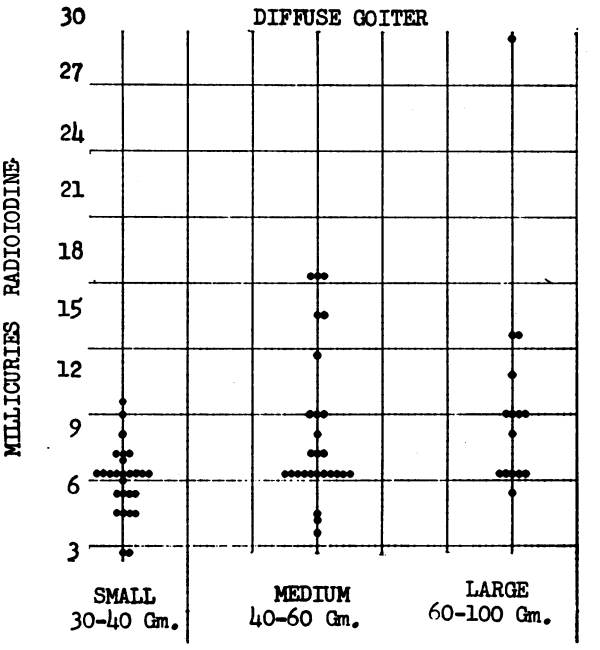

Chart 1.—Dose of I^{131} given for treatment of diffuse thyrotoxic goiters.

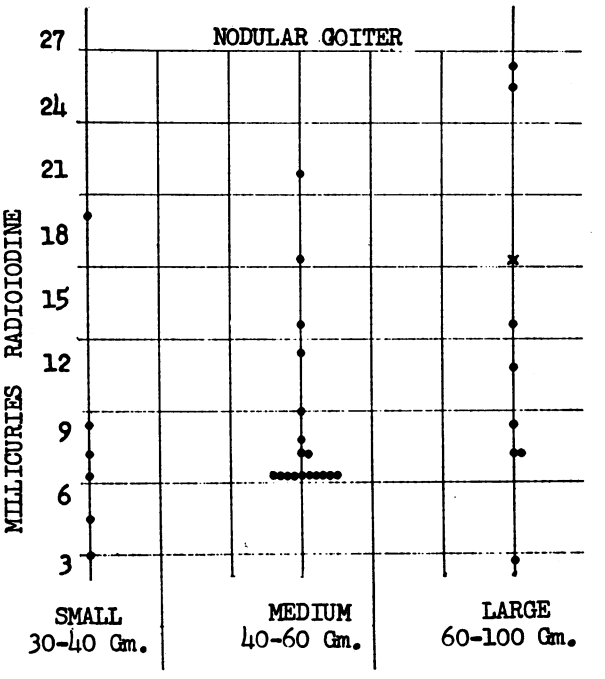

Chart 2.—Dose of I^{131} given for treatment of nodular thyrotoxic goiters.

DISCUSSION

The authors believe that all patients with hyperthyroidism will have response to radioactive iodine therapy if adequately treated. While there are isolated reports of other adverse effects, the authors have observed only hypothyroidism; interestingly enough this occurred in the present series, and in the experience of other investigators working with radioactive iodine,[6] in almost precisely the same percentage as following thyroidectomy.[1] There is obviously no risk of operative death, recurrent laryngeal nerve paralysis or hypoparathyroidism.

Feitelberg and coworkers[2] reported death from a thyroid storm shortly after administration of I^{131} to a patient with a 200-gm. goiter. There is also a report of temporary hyperparathyroidism[8] after radioactive iodine therapy.

The problem of dosimetry is a difficult and frustrating one. One may adopt one of several formulae of calculation based on an estimated weight of the gland involved, the radioactive iodine uptake as determined by an immediately preceding tracer study, and the effective half-life of the isotope. Or one may pass, by way of Seed's[6] lighthearted advice, to the virtual use of a crystal ball. Whatever method of dose determination one seeks to follow, he ultimately comes to agree with Soley and Foreman[7] that "sound clinical judgment rather than simplified formulations" provides the safest guide; and with Seed that there are "no satisfactory criteria for estimating dosage."

When first they used I^{131} the authors employed rough formulation in estimating dosage. Thus, an attempt was made, after palpatory estimation of the size of the gland and after radioactive iodine uptake tests, to deliver 100 to 120 microcuries of I^{131} per gram of the tissue to the thyroid gland. The problems

of such estimates have been well summarized by Kelly.[5] In the last two years, an arbitrary dose of 7 millicuries has been administered to most patients. It is hoped that in subsequent communications results of these two types of approaches to therapy can be compared.

It is impossible to evaluate the differences noted in the various groups as to the number of treatments required. The average initial dose given to those who only required one treatment was 7.2 millicuries, and to those who subsequently required re-treatment, the average initial dose was 7.1 millicuries. The problems of tissue sensitivity, intensity of mechanisms producing the disease, distribution of the radioactive material in the gland, the rapidity of turnover of iodine in the gland, and the size of the gland must influence the amount of radiation delivered. These factors need more careful analysis than has been available to this time in order that dosage may be expressed confidently in terms of equivalent roentgens rather than millicuries.

The average time of remission (reported in a preceding paragraph) is a difficult factor to appraise. The patients in the present series were re-treated in eight to ten weeks if improvement was not noted. It is possible that if there were a longer period of observation, not so many patients would be found to need re-treatment.

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